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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,762	07/23/2001	Roland Schule	SCH-1700 D1	2957

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/909,762	SCHULE ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-14* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 1-7, 9-14 are pending. Claims 10-12 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-7, 9, 13-14 are under consideration.

Response to Amendment

Applicant's amendment and arguments filed 11/18/2003 have been fully considered but they are persuasive in part for the reasons set forth below.

The rejection of claim 13 under 35 USC § 112 second paragraph has been obviated by Applicant's amendment and is thus withdrawn.

Claim Objections

Claims 1-7, 9, 13-14 stand objected to because of the following informalities: They contain subject matter directed to a non-elected invention. In Paper No. 4, 10/9/2002, Applicant elected, with traverse, Group I, drawn to a method of identifying agents that regulate the transcriptional activity of human AR and SLIM3. The restriction was made final in Paper No. 5, 12/31/2002. Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9, 13-14 stand rejected under 35 USC 112 first paragraph because the specification, while being enabling for a method of identifying agents that regulate the transcriptional activating activity of human AR and human SLIM3, does not reasonably provide

enablement for a method of identifying agents that regulate the transcriptional activating activity of biologically active derivatives of human AR and biologically active derivatives of human SLIM3, nor does the specification reasonably provide enablement for a method of identifying agents that regulate the transcriptional activating activity of human AR comprising allelic modifications and human SLIM3 comprising allelic modifications. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

The rejection of record set forth that in the instant case, the claims are directed to a method of identifying agents that regulate the transcriptional activating activity of biologically active derivatives or allelic modifications of human AR and biologically active derivatives or allelic modifications of human SLIM3. Thus, the claims encompass methods using variant proteins. Applicant has only taught the method using human AR and human SLIM3 (page 16, line25 to page 17 line 5). Applicant has provided little or no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may

not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible derivatives or modifications of AR or SLIM3.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives and allelic modifications recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant has amended the claims to now recite that the biologically active derivative is at least 90% identical to SLIM3 and functions as a co-activator for androgen receptor. Applicant argues that the addition of these limitations, and the Specification, provides guidance to enable on e of skill in the art to readily ascertain the possible biologically active derivatives of SLIM3. Applicant further argues that creating mutants of modified proteins is common and well known in the art. However, neither the claims nor specification make clear the sequence of the reference protein to which the biologically active derivatives must be 90% homologous to. The specification sets forth that the SLIM3 protein was described in the Morgan reference (page 1, lines 11-13 and page 4, lines 15-16) however, the specification also sets forth that the SLIM3

protein encompasses allelic variants, deletions, insertions and substitutions (page 4, lines 29-31). The claims as written thus read on a method using a protein that is 90% identical to a protein that is a variant of a protein taught in the art. Thus there is no ascertainable standard by which to determine the actual sequence of the proteins to be used in the claimed method. Since detailed information regarding the structural and functional requirements of the encoded polypeptide is lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass methods using polypeptides which the specification only teaches one skilled in the art to test for functional variants to be used in the claimed method. It would require undue experimentation for one of skill in the art to practice the claimed method, since the skilled artisan would have to first make polypeptide variants of SLIM3, then test for function. Because the amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex, accurate predictions of a polypeptide's structure from mere sequence data are limited. Thus, since Applicant has only taught how to test for polypeptide variants of SLIM3, and has not taught how to make polypeptide variants of SLIM3, it would require undue experimentation of one of skill in the art to practice the claimed method.

Thus, given the breadth of claims 1-7, 9, 13-14 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Claim 13 stands rejected, and claims 1-7, 9, 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The specification sets forth that the SLIM3 protein was described in the Morgan reference (page 1, lines 11-13 and page 4, lines 15-16) however, the specification also sets forth that the SLIM3 protein encompasses allelic variants, deletions, insertions and substitutions (page 4, lines 29-31). The claims as written thus read on a method using a protein that is 90% identical to a protein that is a variant of a protein taught in the art. Thus there is no ascertainable standard by which to determine the actual sequence of the proteins to be used in the claimed method. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the reference SLIM3 polypeptide. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No

common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the SLIM3 polypeptide alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Additionally, claim 13 recites the limitation wherein the protein is an "allelic derivative", thus a determination of what the claim as a whole covers indicates that elements that are not particularly described, e.g. the sequence of the claimed allelic modifications, are encompassed by this claim. There is no actual reduction to practice of the claimed invention, or complete detailed description of the structure. Alleles are two or more alternative forms of a gene occupying the same locus on a particular chromosome, and differing from other alleles of that locus at one or more mutational sites. In the instant case the structure of the allelic modifications are not defined. The skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Applicant argues that Applicant's have satisfied the written description requirement by disclosing relevant identifying characteristics, i.e. a function with a correlation between structure and function. Applicant additionally argues that the instant claims are analogous to Example 14 of the Written Description Guidelines in that the claim is drawn to methods using variants that are structurally similar to the disclosed sequence and possess the same function as the disclosed

protein. However, in the instant case, the claims read on methods using a protein which is 90% identical to a variant of a protein taught in the art. There is no standard set forth, for which the reference protein may differ from the SLIM3 protein as taught in the art. Since the reference protein need only be 90% identical to the reference protein and the reference protein is a variant of SLIM3, there is not an adequate correlation between the structure and function of the encompassed variant protein, because there is not an ascertainable structure for the SLIM3 protein variant. Thus, Applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-7, 9 and 13 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,789,170 (Chang et al.), for reasons of record set forth in Paper No. 5, 12/31/2002 and the Office action of 7/28/2003. U.S. Patent No. 5,789,170 has a priority date of May 23, 1996.

U.S. Patent no. 5, 789, 170 discloses the cloning and expression of a co-activator of human androgen receptor, ARA70 (column 2, lines 6-16). Based on the limitation "biologically active derivative" in claim 1, and the term "allelic modification" in claim 13, ARA 70 can be considered a biologically active derivative or allelic modification of SLIM3. U.S. Patent No. 5, 789,170 also discloses methods of screening for ligands which regulate transcriptional activity of androgen receptor in the presence of ARA70, (column 6, lines 3-15) in the yeast two-hybrid system, using AR-GAL4 binding domain fusion constructs and ARA70-GAL4 activator domain fusion constructs (column 4, lines 23-35, see also Figure 1). Thus claims 1-7, 9, 13 are anticipated.

Applicant argues that the ARA70 protein is not at least 90% homologous to SLIM3, and is not a co-activator for ER-beta. However, the specification also sets forth that the SLIM3 protein encompasses allelic variants, deletions, insertions and substitutions (page 4, lines 29-31). The claims as written thus read on a method using a protein that is 90% identical to a protein that is a variant of a protein taught in the art. Thus there is no standard by which to determine the actual sequence of the proteins to be used in the claimed method. Additionally, the ARA70 protein is taught as interacting with the AR. Thus, since the ARA70 protein cannot be

distinguished from the SLIM3 protein based on either structural or functional indicia, therefore the claims are anticipated by the '170 patent.

Claims 1, 3, 9, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Culig et al. (1994), for reasons of record set forth in the Office action of 7/28/2003.

Culig et al. teaches a method of measuring the effect of various compounds on the transcriptional activity of androgen receptor transfected and expressed in DU-145 cells (page 5475, Figures 1 and 2). The cells used in the method of Culig, DU-145 cells, are a prostatic tumor cell line (page 5474, column 1, second paragraph). According to the Specification, SLIM-3 is expressed in the prostate (Specification at 1, line 16). Thus, Culig et al. teaches a method of identifying agents which regulate the transcriptional activity of AR in cells expressing both AR and SLIM-3 by measuring the transcriptional activity of AR, thus claims 1, 13-14 are anticipated. The transcriptional activity of AR is indicated by measuring the transcription of CAT, thus claim 3 is anticipated. Claim 9 is anticipated because several of the agents assayed in Culig et al. function as agonists (e.g., see page 5475, Figure 1, R1881 and IGF-1).

Applicant argues that Culig et al. does not teach a protein at least 90% homologous to SLIM3 which also functions as a co-activator of AR and ER-beta. However, the specification also sets forth that the SLIM3 protein encompasses allelic variants, deletions, insertions and substitutions (page 4, lines 29-31). The claims as written thus read on a method using a protein that is 90% identical to a protein that is a variant of a protein taught in the art. Thus there is no standard by which to determine the actual sequence of the proteins to be used in the claimed method. Additionally, the method taught in Culig et al. determines the effect of agents on the

transcriptional activity of AR by contacting a cell expressing AR and SLIM3 with the agent. This meets all the limitations of the claims, thus the claims are anticipated.

Conclusion

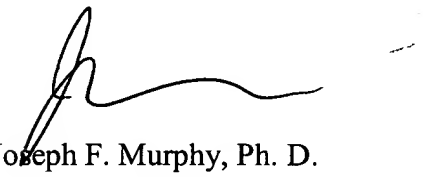
No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



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Patent Examiner
Art Unit 1646
January 29, 2004